

### LISTING OF CLAIMS

1. *(original)* An isolated, recombinant polypeptide molecule comprising a first amino acid sequence which is a fragment of a native proteolipid protein having a wild type or mutant sequence as compared with the native sequence of said proteolipid protein, and optionally comprising a second amino acid sequence fused in frame thereto to create a fusion polypeptide, which first polypeptide is encoded by an mRNA having an Internal Ribosome Entry Site ((IRES) wherein translation of the mRNA initiates at said IRES, such that the N-terminal amino acid residue of said first polypeptide corresponds to an internal residue of said proteolipid protein.
2. *(currently amended)* The polypeptide of claim 1 [[or]] wherein the proteolipid protein is human PLP/DM20.
3. *(currently amended)* The first polypeptide or of claim 1 selected from the group consisting of:
  - (a) PIRP-M, having the amino acid sequence SEQ ID NO:6;
  - (b) PIRP-L, having the amino acid sequence SEQ ID NO:8;
  - (c) a fusion polypeptide of (a) or (b) wherein said second amino acid sequence encodes a naturally fluorescent protein or peptide;
  - (d) a His-tagged fusion polypeptide of PIRP-M having the amino acid sequence SEQ ID NO:12;
  - (e) a His-tagged fusion polypeptide of PIRP-L having the amino acid sequence SEQ ID NO:16; and
  - (f) PIRP-J having a mutant sequence compared to said proteolipid protein, the sequence of said PIRP-J being SEQ ID NO:18, or a human homologue thereof.
4. *(original)* The polypeptide of claim 3 which is PIRP-M having the amino acid sequence SEQ ID NO:6
5. *(original)* The polypeptide of claim 3 which is PIRP-L, having the amino acid sequence SEQ ID NO:8.
6. *(original)* The polypeptide of claim 3 which is PIRP-J having the amino acid sequence SEQ ID NO:18.

7. *(currently amended)* The fusion polypeptide of claim 3 wherein said fluorescent protein is yellow or ~~green~~ green fluorescent protein (GFP) or a fluorescent homologue thereof.
8. *(original)* The His-tagged fusion polypeptide of claim 3 having the sequence SEQ ID NO:12.
9. *(original)* The His-tagged fusion polypeptide of claim 3 having the sequence SEQ ID NO:16.
10. *(original)* An isolated nucleic acid encoding the polypeptide of claim 1, the mutant sequence thereof, or the fusion polypeptide thereof.
11. *(original)* The nucleic acid of claim 10 which is a DNA molecule.
12. *(original)* The nucleic acid of claim 10 which is an RNA molecule.
13. *(original)* The nucleic acid of claim 10 wherein the proteolipid protein is human PLP/DM20.
14. *(original)* The nucleic acid of claim 10 encoding a polypeptide or fusion polypeptide selected from the group consisting of:
  - (a) PIRP-M, having the amino acid sequence SEQ ID NO:6;
  - (b) PIRP-L, having the amino acid sequence SEQ ID NO:8;
  - (c) a fusion polypeptide of (a) or (b) wherein said second amino acid sequence encodes a naturally fluorescent protein or peptide;
  - (d) a His-tagged fusion polypeptide of PIRP-M having the amino acid sequence SEQ ID NO:12;
  - (e) a His-tagged fusion polypeptide of PIRP-L having the amino acid sequence SEQ ID NO:16; and
  - (f) PIRP-J having a mutant sequence compared to said proteolipid protein, the sequence of said PIRP-J being SEQ ID NO:18, or a human homologue thereof.
15. *(original)* The nucleic acid of claim 14 which encodes PIRP-M and has a nucleotide sequence SEQ ID NO:5 or SEQ ID NO:9.
16. *(original)* The nucleic acid of claim 14 which encodes PIRP-L and has a nucleotide sequence SEQ ID NO:7 or SEQ ID NO:13.

17. *(original)* The nucleic acid of claim 14 which encodes PIRP-J and has a nucleotide sequence SEQ ID NO:17.

18. *(original)* The nucleic acid of claim 14 which encodes said His-tagged fusion polypeptide of PIRP-M, which nucleic acid has a nucleotide sequence SEQ ID NO:11;

19. *(original)* The nucleic acid of claim 14 which encodes said His-tagged fusion polypeptide of PIRP-L, which nucleic acid has a nucleotide sequence SEQ ID NO:15;

20. *(original)* The nucleic acid of claim 14 which encodes said fusion polypeptide wherein said second amino acid sequence encodes a naturally fluorescent protein or peptide.

21. *(currently amended)* The nucleic acid of claim 20 wherein said fluorescent protein is yellow or ~~green~~ green fluorescent protein (GFP) or a fluorescent homologue thereof.

22. *(currently amended)* The nucleic acid ~~molecule~~ of ~~any of claims~~ claim 10[[-21]] operatively linked to a promoter.

23. *(currently amended)* The nucleic acid ~~molecule~~ of claim 22, wherein the promoter is one which is expressed in a mammalian cell.

24. *(currently amended)* The nucleic acid ~~molecule~~ of claim 23 wherein said mammalian cell is a neuronal cell, a glial cell or a stem cell.

25. *(currently amended)* The nucleic acid ~~molecule~~ of claim 24 wherein said glial cell is an oligodendrocyte.

26. *(currently amended)* The nucleic acid ~~molecule~~ of claim 24 wherein the stem cell is a neural stem cell, an oligodendrocyte progenitor cell, an embryonic stem cell or a hemopoietic stem cell.

27. *(currently amended)* A vector comprising the nucleic acid of ~~any of claims~~ claim 10 [[-21]].

28. *(original)* The vector of claim 27, selected from the group consisting of PLP-GFP/DM20-GFP; PLP-GFP/DM20-GFP Tet-On; PLP-GFP/DM20-GFP M1L; PLP-GFP/DM20-GFP M1L/M205L; PLP-GFP/DM20-GFP M1L/M234L; PLP-GFP/DM20-GFP M1L/M205L/M234L; PLP-GFP/DM20-GFP Pro-; JPLP-GFP/JDM20-GFP; JPLP-GFP/JDM20-GFP M1L;

JPLP-GFP/JDM20-GFP M1L/M205L; RshPLP-GFP/RshDM20-GFP M1L; PLP-GFP/DM20-GFP M1L/K268R; PLP-GFP/DM20-GFP M1L/K275R; PLP-GFP/DM20-GFP M1L/K268R/K275R; and PLP-GFP/DM20-GFP M1L/R272K

29. (*currently amended*) An expression vector or cassette comprising the nucleic acid of ~~any of~~ claims claim 10[[-21]] operatively linked to

- (a) a promoter; and
- (b) optionally, additional regulatory sequences that regulate expression of said nucleic acid in a eukaryotic cell.

30. (*original*) The expression vector or cassette of claim 27 comprising a vector selected from the group consisting of pCMV; pEGFP-N1; pEYFP-N1; pEGFP-Tet-On; pBluescript II KS+; and pET-14b.

31. (*original*) The expression vector or cassette of claim 28 elected from the group consisting of 205M-CMV/234M-CMV; 205M-His-CMV/234M-His-CMV; 205M-BsKS+/234M-BsKS+; 205M-His-BsKS+/ 234M-His-BsKS+; and 205M-ET-14b/234M-ET-14b.

32. (*currently amended*) A cell which has been modified to comprise the nucleic acid of ~~any of~~ claims claim 10[[-21]].

33. (*original*) The cell of claim 32 which is a mammalian cell.

34. (*original*) A cell which has been modified to comprise the vector of claim 27.

35. (*original*) A cell which has been modified to comprise the vector or expression cassette of claim 31.

36. (*currently amended*) The cell of claim 35 which expresses said nucleic acid ~~molecule~~.

37. (*original*) The cell of claim 36 which is mammalian cell.

38. (*original*) The cell of claim 37 wherein said mammalian cell is a neuronal cell, a glial cell or a stem cell.

39. (*original*) The cell of claim 38 wherein said glial cell is an oligodendrocyte.

40. *(original)* The cells of claim 38 wherein the stem cell is a neural stem cell, an oligodendrocyte progenitor cell, an embryonic stem cell or a hemopoietic stem cell.

41. *(currently amended)* A pharmaceutical composition, comprising:

- (a) pharmaceutically acceptable excipient in combination with
- (b) the polypeptide of ~~any of claims~~ claim 1[[-6]].

42. *(currently amended)* A pharmaceutical composition, comprising:

- (a) pharmaceutically acceptable excipient in combination with
- (b) the nucleic acid ~~molecule~~ of claim[[s]] 23.

43. *(original)* A pharmaceutical composition, comprising:

- (a) pharmaceutically acceptable excipient in combination with
- (b) the expression vector or cassette of claim 29;

44. *(original)* A pharmaceutical composition, comprising:

- (a) pharmaceutically acceptable excipient in combination with
- (b) the cell of claim 33.

45. **CANCEL**

46. *(new)* A method for stimulating oligodendroglial cells or Schwann cells and promoting remyelination, comprising providing to said cells an effective amount of the polypeptide of claim 4 or a functional derivative thereof, thereby stimulating said cells and promoting remyelination.

47. *(new)* The method of claim 46 that is carried out *in vivo* in a mammalian subject in need of remyelination.

48. *(new)* A method of treating a demyelinating or dysmyelinating disease or disorder in a mammalian subject, comprising administering to said subject

- (i) the polypeptide of claim 4 or a functional derivative thereof, or
- (ii) a pharmaceutical composition comprising said polypeptide or functional derivative, thereby treating said disease or disorder.

49. *(new)* The method of claim 48, wherein the disease or disorder is multiple sclerosis, closed head trauma associated with Parkinson's-like symptoms, hypoxic ischemia, or spinal cord trauma.

50. *(new)* A method for stimulating oligodendroglial cells or Schwann cells and promoting remyelination in a subject, comprising administering to a subject in need of remyelination an effective amount of the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:5 or SEQ ID NO:9; or
- (ii) encodes a polypeptide having the amino acid sequence SEQ ID NO:6,

thereby promoting said remyelination.

51. *(new)* A method of treating a demyelinating or dysmyelinating disease or disorder in a mammalian subject, comprising administering to said subject the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:5 or SEQ ID NO:9; or
- (ii) encodes a polypeptide having the amino acid sequence SEQ ID NO:6,

thereby treating said disease or disorder.

52. *(new)* A method of stimulating neural stem cell survival and promoting differentiation or maturation of said cells along the oligodendrocyte pathway, comprising providing to said neural stem cells an effective amount of the polypeptide of claim 4 or a functional derivative thereof.

53. *(new)* A method for stimulating proliferation of oligodendrocytes and/or oligodendrocyte precursors, comprising providing to said oligodendrocytes and/or precursors an effective amount of the polypeptide of claim 4 or a functional derivative thereof.

54. *(new)* A method of protecting oligodendrocytes from apoptotic death comprising providing to oligodendrocytes an effective amount of the polypeptide of claim 4 or a functional derivative thereof.

55. *(new)* A method for treating a disease or disorder in which one or more of oligodendrocytic (a) differentiation, (b) maturation, (c) proliferation, and (d) inhibition of cell death is palliative or curative for said disease or disorder, comprising administering to a subject in need of such treatment an effective amount of

- (i) the polypeptide of claim 4 or a functional derivative thereof, or
- (ii) a pharmaceutical composition comprising said polypeptide or functional derivative, thereby treating said disease or disorder.

56. *(new)* A method for treating a disease or disorder in which one or more of oligodendrocytic (a) differentiation, (b) maturation, (c) proliferation, and (d) inhibition of cell death is palliative or curative for said disease or disorder, comprising administering to a subject in need of such treatment an effective amount of the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:5 or SEQ ID NO:9; or
  - (ii) encodes a polypeptide having the amino acid sequence SEQ ID NO:6,
- thereby treating said disease or disorder.

57. *(new)* A method for regulating or inhibiting the production or action of PLP/DM20 or of PIRP-M polypeptide under conditions in which said PLP/DM20 or PIRP-M is pathogenically produced in cells or in a subject, comprising providing to the cells or to the subject an effective amount of the polypeptide of claim 5 or a functional derivative thereof.

58. *(new)* The method of claim 57 wherein the polypeptide or functional derivative is administered to a subject with oligodendroglioma or a benign glial tumor

59. *(new)* A method for regulating or inhibiting the production or action of PLP/DM20 or of PIRP-M polypeptide under conditions in which said PLP/DM20 or PIRP-M is pathogenically produced in cells or in a subject, comprising providing to the cells or to the subject an effective amount of the cells of claim 32 which have been modified by said nucleic acid that

- (i) has a nucleotide sequence SEQ ID NO:7 or SEQ ID NO:13, or
- (ii) encodes a polypeptide comprising an amino acid sequence SEQ ID NO:8.

60. *(new)* The method of claim 59 wherein the cells being provided are administered to a subject with oligodendroglioma or a benign glial tumor.